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| 10/608,915      | 06/27/2003  | Stephen L. Hoffman   | ABIOS.023A          | 7068             |

  

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| WHALEY, PABLO S |  |

  

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| ART UNIT | PAPER NUMBER |
| 1631     |              |

  

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| NOTIFICATION DATE | DELIVERY MODE |
| 07/06/2007        | ELECTRONIC    |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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# Office Action Summary

Application No.

10/608,915

Applicant(s)

HOFFMAN, STEPHEN

Examiner

Pablo Whaley

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 25 April 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 85-115 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 85-92 and 107-115 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## DETAILED ACTION

Applicants' remarks, filed 04/25/2007, have been fully considered. The following rejections and/or objections are maintained, newly applied, or withdrawn for the reasons set forth below. They constitute the complete set presently being applied to the instant application.

### *CLAIMS UNDER EXAMINATION*

Claims herein under examination are Claims 85-92 and 107-115.

Claims 1-84 have been cancelled. Claims 112-115 are newly added. This application contains claims 93-106 drawn to an invention nonelected with traverse in the response filed 12/27/2005. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

### *APPLICANTS' ELECTION*

Applicants' election without traverse of Group I drawn to Claims 85-92, 107 and 108, and election of Species I (iii), Species II (iii), and Species III (i) with traverse, filed 12/27/2005, is reiterated. The specie election requirement has been withdrawn for Specie II and III, and is hereby withdrawn for Specie I as the Examiner has determined this is not a search burden. Claims 93-106 are hereby withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/27/2005.

### *INFORMALITIES*

The amended disclosure is acceptable, as it no longer contains contains an embedded hyperlink and/or other form of browser-executable code on pages 39, 40, and elsewhere.

***CLAIM REJECTIONS - 35 USC § 112, 2<sup>nd</sup> Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 85-92 and 114-115 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims that depend directly or indirectly from claims 85 and 90 are also reject due to said dependence.

Claims 85 and 90 recite "outputting a product." It is unclear what "product" applicant is referring to. Clarification is requested via clearer claim language.

***NEW MATTER***

Claims 85 and 107-111 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Applicant's arguments are persuasive. This rejection is hereby withdrawn.

**CLAIM REJECTIONS - 35 USC § 101**

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 85-92 were rejected and claims 107-111 remain rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter.

Applicant's arguments that claims 85-92 are now statutory are persuasive in view of the amendment to claim 85, which now recites a step of outputting data. This rejection is hereby withdrawn for claims 85-92.

Applicant's arguments that claims 107-111 are now statutory are not persuasive for the following reasons. According to the revised Guidelines, a claimed invention directed to a statutory process must provide: (1) a practical application by physical transformation (i.e. reduction of an article to a different state or thing), or (2) a practical application that produces a concrete, tangible, and useful result [State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998)], [AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999))]. The revised Guidelines also state that the focus is "not on whether the steps taken to achieve a particular result are useful, tangible, and concrete, but rather on whether the final result achieved by the claimed invention is useful, tangible, and concrete." In view of the revised Guidelines, and in view of the amendment to claim 107, the Examiner maintains that the claimed method does not result in a physical transformation of matter, as the limitation "wherein said...prediction is performed on a computer" may conceivably be practice inside of a computer. Where a claimed method does not result in a physical transformation of matter, it may be statutory where it recites a result that is concrete (i.e. reproducible), tangible (i.e. real world), and useful result (i.e. a specific and substantial). However, claim 107 clearly results in a step of "evaluating" and thus does not recite a tangible result such that it is useful to one skilled in the art. For these reasons, this rejection is maintained.

This rejection could be overcome by amending the claims to recite a "tangible" (i.e. real-world result). For exemplary purposes only, applicant would likely overcome this rejection by amending the claims to recite one of the following: (1) a step wherein the result of the claimed method is communicated to a user (i.e. real-world result), graphically displayed, or output (e.g. to a user, to a memory, or to another computer); or (2) by amending the claims to include of a physical transformation of matter (e.g. assay). For an updated discussion of statutory considerations, see the revised Guidelines for Patent Eligible Subject Matter in the MPEP 2106, Section IV (Latest Revision August 2006).

#### **CLAIM REJECTIONS - 35 USC §112, 1<sup>st</sup> Paragraph**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 85-92 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicant's arguments, filed 04/25/2007, that the instant claims are enabled in view of the amendments to claims 85 and 90 and in view of the teachings of the prior art are persuasive. This rejection is hereby withdrawn.

### **CLAIM REJECTIONS - 35 USC § 102**

Claims 85, 87-90, and 92 were rejected under 35 U.S.C. 102 (b) as being anticipated by Yaffe et al. (Nature Biotechnology, April 2001, Vol. 19, p.348-353). Applicant's arguments, filed 04/25/2007, that Yaffe et al. do not teach two distinct predictive methods are persuasive. This rejection is hereby withdrawn.

Claims 85, 86, 90, 91, 107, 109-111 were rejected under 35 U.S.C. 102 (b) as being anticipated by Mamitsuka (Proteins: Structure, Function, and Genetics, 1998, Vol. 33, p.460-474). Applicant's arguments, filed 04/25/2007, that Mamitsuka et al. do not teach two distinct predictive methods are persuasive. This rejection is hereby withdrawn.

### **Claim Rejections - 35 USC § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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Claims 85-92 and 109-115 are rejected under 35 U.S.C. 103(a) as being obvious by Rognan et al. (J. Med. Chem., 1999, Vol. 42, p.4650-4658), in view of Yaffe et al. (Nature Biotechnology, April 2001, Vol. 19, p.348-353). *This rejection is necessitated by amendment.*

Rognan et al. teach structure-based method for predicting the binding free energy of candidate peptides to MHC class I proteins [Abstract], as set forth in the previous office action mailed 08/09/2006. More specifically, Rognan et al. teach the following aspects of the instantly claimed invention: a database of MHC proteins and MHC-bound candidate peptides [Fig. 1]; determining binding scores (i.e. affinities) using a predictive method that incorporates linear equations [Fig. 1]; linear regression analysis (i.e. linear scaling) of the affinity data from each scoring model before they are combined [p.4657, Statistical Analyses]; normalization (i.e. scaling) of data values between 0 and 1 [Fig. 4], and combining affinity data to determine a single predictive binding affinity [Fig. 1], as in instant claims 85, 87, 89, 90, 92, 109-112. As the Specification teaches scoring by individual methods and combining "scores" to determine an overall ranking for peptide binding [Specification, Fig. 2 and 3], the above method taught by Rognan et al. is reasonably interpreted as five distinct methods of predictive scoring to determine an overall predictive score. Rognan et al. also teaches specific antigen binding domains for MHC proteins [p.4655, Col. 2, ¶ 1], which is a teaching for epitopes, as in claims 86 and 91, which are well-known to bind to MHC proteins. Rognan et al. also teach a predictive model applied to nonameric ligands [p.4654, Col. 2, 2], as in instant claim 88. Rognan et al. also teach mathematical functions and computing protocols for carrying out the above method [p.4566, Experimental Section] and displaying results [Fig. 3], which is an implicit teaching for outputting results and a user and a memory, as in claims 95, 90, 107-112, 114, and 115.



Rognan et al. do not specifically teach the use of a second predictive method for determining a second affinity of a candidate for a target protein, as in instant claims 85, 90, and 107-112. However, Rognan et al. do suggest the use of their method with proteins that have well-known binding motifs [p.4653, Col. 2, ¶ 2].

Yaffe et al. teach a profile-based method for predicting protein-protein interactions [Abstract], as set forth in the previous office action mailed 02/01/2007. More specifically, Yaffe et al. teach the following aspects of the instant claims:

- Obtaining known peptide sequence data and surface accessibility values (i.e. binding information) [p.353, Col. 1, ¶ 3], as in claim 85, 90.
- Scanning of a protein to obtain potential peptide binding motifs (i.e. candidate peptides), as in claims 85, 90.
- Profile-based scoring algorithm comprising bit scores (i.e. first affinity) calculated for putative motifs domains using a first equation (i.e. first predictive method) [p.349, Col. 1, ¶ 1] that employs sequence information from experimental data [p.353, Col. 1, ¶ 3], as in claims 85, 89, and 92.
- Profile-based scoring algorithm also comprising raw sequence scores (i.e. second affinity) calculated using a second equation [p.349, Col. 1, ¶ 1] and [Fig. 3] that employs and compares sequence information from putative motifs and experimental data [p.353, Col. 1, ¶ 3], as in claims 85, 90.
- Normalizing (i.e. scaling) bit scores and raw sequence scores [p.349, Col. 1, ¶ 1], which inherently results in values between 0 and 1, as in claims 85, 87, 90.
- Combining normalized raw scores and optimal scores to calculate a final sequence score ( $S_f$ ), wherein final sequence score is used for assessing the affinity between putative motifs and a target sequence [p.349, Col. 1, ¶ 1], as in claim 85.

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- Screening motif wherein motif sequence data is divided into nine-mers or ten-mers [p.350, Col. 2, ¶ 2], as in claim 88.
- Using “final sequence scores” for calculating a percentile rank (i.e. vote) based on said [p.350, Col. 1, ¶ 1] and [Fig. 2], as in claim 90. As final sequence scores inherently contains combined normalized values, the Examiner has interpreted this as a teaching for “combining the first and second votes” as in claim 90.
- A Scansite web-based program that graphically displays results that are output from the program to a user on a computer [Fig. 1], as in claims 95, 90, 107-112, 114, and 115.

To address applicant's arguments that the Examiner has not provided any reasoning to demonstrate why “scores” taught in Yaffe et al. would equate to affinities of a candidate peptide for a target peptide, it is noted that Yaffe et al. clearly teach a profile scanning algorithm that evaluates individual protein sequences or entire databases (i.e. target peptides) via a Web-based program and returns a list of top-ranking matches for protein signaling motifs (i.e. candidate peptides) as well as a site score that describes the quality of the match [p. 348, Col. 1, ¶ 3]. Therefore the Examiner has broadly interpreted the matching and site “scores” of Yaffe et al. as a teaching for “affinities.”

Thus it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the structure-based predictive method taught by Rognan et al. in combination with the motif-based predictive algorithm taught by Yaffe et al., as Rognan et al. suggest combining sequence homology data with their method [Fig. 1 and p.4644, Col. 1, ¶ 3]. One of ordinary skill in the art would have been motivated to combine the above teachings to develop an improved method of scanning for MHC-binders and T-cell epitopes [Rognan et al., Conclusion], resulting in the practice of the instant claimed invention. One of ordinary skill in the

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art would have had a reasonable expectation of successfully combining the above teachings as both Rognan et al. and Yaffe et al. both teach predictive binding methods applied to protein data.

Claims 85, 87-90, 92, and 109-115 are rejected under 35 U.S.C. 103(a) as being made obvious by Yaffe et al. (Nature Biotechnology, April 2001, Vol. 19, p.348-353), in view of Geetha et al. (Protein Engineering, 1999, Vol. 12, No. 7, p.527-534). *This rejection is necessitated by amendment.*

Yaffe et al. teach a profile-based scanning algorithm that evaluates individual protein sequences or entire databases (i.e. target peptides) via a Web-based program, and returns a list of top-ranking matches for protein signaling motifs (i.e. candidate peptides) as well as a site score that describes the quality of the match [p. 348, Col. 1, ¶ 3], as set forth above and as in claims 85, 87-90, 92, and 109-115.

Yaffe et al. do not specifically teach a second predictive algorithm or assessing binding affinity as a basis of a first and second affinity, as in claims 85, 90, and 109-113. However, Yaffe et al. do compare their method to structure-based predictive methods [p.352, Col. 2, ¶ 3].

Geetha et al. teach methods for comparing protein-based and structure-based methods for detecting remote homologs [Abstract]. More specifically, Geetha et al. provide structure-based predictive methods (i.e. FORESST) for evaluating binding capabilities based on quadratic programming [p.530, Col. 1, ¶ 2] and calculation of Z-scores that determine the affinity of a match between candidate and target proteins [p.529, Col. 1, ¶ 2], as in claims 85, 90, and 109-113.

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Thus it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to combine the profile-based method of Yaffe et al. with the structure-based method taught by Geetha et al., where the motivation would have been to improve binding affinity prediction using a model that incorporates sequence and structural predictive methods [Geetha et al., Conclusion], resulting in the practice of the instantly claimed invention. One of ordinary skill in the art would have had a reasonable expectation of successfully combining the above teachings as Geetha et al. clearly teach both sequence-based and structure-based predictive binding methods applied to protein data.

#### CONCLUSION

No claims are allowed.

Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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